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Chemical Category	CAB-O-SIL N70-TS				

Hoechst Celanese

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Department of
Environmental, Health &
Safety Affairs (DEHSA)

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November 6, 1992
RAJ-169-92

Document Processing Center (TS-790)
U.S. Environmental Protection Agency
401 M St., S.W.
Washington, D.C. 20460
Attn: TSCA Section 8(e) Coordinator

Dear Sir or Madam:

In accordance with the requirements of TSCA Section 8(e), Hoechst Celanese Corporation hereby submits a report of a 28 day dust inhalation study in rats of CAB-O-SIL® TS-720, treated fumed silica (CAS No. 67762-90-7). The chemical identity given in the report CAB-O-SIL N70-TS, according to Cabot Corporation, is identical to CAB-O-SIL® TS-720. The toxicity report was recently obtained from Cabot Corporation.

In this study, 40 male and 40 female rats were exposed to CAB-O-SIL® TS-720, Treated Fumed Silica at a concentration of 60 mg/m^3 for 6 h/day, 5 days/week for up to 4 weeks. During the first day of treatment, signs of excessive toxicity were observed and a decision was made to reduce the exposure to 30 mg/m^3 for the remainder of the experiment. Despite this adjustment, by the end of treatment day 2, nine male rats had died. Necropsy of these animals revealed evidence of a lethal, acute pulmonary hemorrhage accompanied by bronchiolar plugs with emphysema in five out of five rats examined. The acute toxicity exhibited by this surface-altered material is much greater than would be expected for untreated amorphous silica.

CAB-O-SIL® TS-720, Treated Fumed Silica is being investigated by the Hoechst Celanese Corporation for use as an additive in polymeric materials. Once the polymers are manufactured, the treated fumed silica is incorporated into the polymer matrix presenting no opportunity for consumer exposure. Hoechst Celanese Corporation will take adequate measures to protect its workers from excessive exposure to this material.

This submission contains no confidential business information.

If any further information is required, do not hesitate to contact Dr. Michele R. Sullivan, Director, Product Safety at (908) 231-4480.

Sincerely,

Susan Engelman
Vice President, Environmental, Health & Safety Affairs

CERTIFIED MAIL/
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Hoechst

TOXIGENICS' STUDY 420-1171

28-DAY DUST INHALATION TOXICITY STUDY OF CAB-O-SIL N70-TS IN ALBINO RATS

SUBMITTED TO:

CABOT CORPORATION
CAB-O-SIL DIVISION
P.O. BOX 188
TUSCOLA, IL 61953

SUBMITTED BY:

TOXIGENICS, INC.
1800 EAST PERSHING ROAD
DECATUR, IL 62526

JUNE 29, 1983

Study No. 420-1171

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

LIST OF TABLES

Tables

LIST OF APPENDICES

LIST OF APPENDICES (continued)

I. Summary

A 28-day dust inhalation toxicity study using albino rats was conducted with CAB-O-SIL N70-TS. Exposures were for 5 days per week for 4 consecutive weeks.

Four designated groups, T-I, T-II, T-III and T-IV, each consisting of 10 male and 10 female rats, were exposed to an atmosphere of the test article. After weeks 1, 2 and 4, groups T-I, T-II and T-IV, respectively, were sacrificed and examined. The time-weighted average (cumulated) gravimetric concentrations for weeks 1, 2, 3 and 4 of the study were; 0.037, 0.031, 0.031 and 0.031 mg/l air, respectively. Two Vehicle Control groups, VC-I and VC-II, were exposed to air only and were sacrificed and examined after 2 and 4 weeks, respectively, of exposure. Each Vehicle Control group consisted of 10 males and 10 females. Test group T-III was designated a recovery group with one-half (5 males and 5 females) sacrificed after 6 and 12 weeks, respectively, of recovery. (Following 4 weeks of exposure.)

The 6- and 12-week recovery groups will henceforth be referred to as T-IIIA and T-IIIB, respectively.

During the first 2 days of the study, 9 male rats died. This was apparently due to test article at a level of 0.06 mg/l air during the firt six hours of the study (day 1). Subsequently, test article target concentration was set at 0.03 mg/l air.

Animal observations noted included; crusty eye, crusty muzzle, crusty nose, crusty substance around ear tag, eye closed,

irregular breathing, irritable, lacrimation, salivation, scab, red stained fur and yellow/brown stained fur.

Mean body weights of test animals did not differ statistically from corresponding controls during the course of the study. Recovery group animals appeared to gain weight at a rate comparable to untreated animals of the same species and strain.

Hematology data indicated a decrease in the relative number of lymphocytes and an increase in the number of neutrophils after 2 and 4 weeks of exposure. This finding is consistent with the chronic-active pulmonary inflammatory process seen histologically. At week four there was an increase in total leukocyte count.

Serum chemistry data were not remarkably different from comparable controls.

Histological examinations of rats exposed to CAB-O-SIL N70-TS at 0.06 mg/l air for six hours followed by an exposure level of 0.031 mg/l air for various times up to 4 weeks was associated with a chronic-active pulmonary inflammatory process. Six weeks after the four weeks of exposure the pulmonary inflammation was more localized and less fulminant. Twelve weeks after the four weeks of exposure, the pulmonary inflammation was even more localized, however histologic markers of chronicity were evident; namely interstitial fibrosis and interstitial collagen proliferation. Granulomatous responses were not seen.

What proportions of the chronic pulmonary lesions were due to the initial severe injury relative to the subsequent lower

dose level (0.060 mg/l air compared to 0.031 mg/l air) cannot be determined from this data.

B. Richard Dudek 6/29/83

B. Richard Dudek, Ph.D. Date
Study Director

6/29/83

Stephen V. Becker, D.V.M. Date
Pathologist

All work relating to this study was done in conformity with the FDA - Good Laboratory Practice Regulations (21 CFR 58). The study was inspected by a Quality Assurance Specialist on the dates shown below. Management, including the Study Director, was informed of the results of these inspections/audits on the dates shown. The data in the report were compared with the raw data and are in agreement. The report and study file were examined to assure that any problems found during Quality Assurance inspections were corrected, and if necessary, their effect on the study documented.

Phase inspections conducted January 21 and 24, 1983.

Final Data Inspection and Report Audit - conducted June 15, 16, 17, and 20, 1983; reported to Management, including the Study Director, June 21, 1983.

Bernard R. Szyszko 6/29/83

Bernard R. Szyszko, B.A., M.T. Date
Supervisor, Quality Assurance

The raw data relating to this study, as well as specimens, and the final report are stored at ToxiGenics, Inc. Storage is as per FDA GLP's and may include volume reduction by conversion to certified microform.

Date of Report: June 29, 1983

II. Introduction

A 28-day inhalation study was conducted in rats to determine the subchronic toxicity of CAB-O-SIL N70-TS. The exposure regimen for this study was 6 hours per day, 5 days per week for a total of 28 days. During the 28-day exposure period, groups of 20 animals (10 males and 10 females) were scheduled for sacrifice and evaluation after 5, 10 and 20 exposures. These groups were designated T-I, T-II and T-IV, respectively. One group, T-III, of 20 rats (10 males and 10

females) was designated as a recovery group with one half of its animals (5 males and 5 females) sacrificed after 6 and 12 weeks of recovery. These groups were designated T-IIIA and T-IIIB, respectively. Given below are the study groups and their scheduled evaluations.

Group	Rats M/F	Clinical Pathology Weeks	Body Weight Weeks	Necropsy Weeks	Initial Histology
Baseline	10/10	0	-	-	-
VC-I	10/10	2	0,1,2	2	
VC-II	10/10	4	0,1,2,3,4	4	X
T-I	10/10	1	0,1	1	
T-II	10/10	2	0,1,2	2	
T-IIIA	5/5	10	0,1,2,3,4-10	10	
T-IIIB	5/5	16	0,1,2,3,4-16	16	
T-IV	10/10	4	0,1,2,3,4	4	X

VC = Vehicle control, air only
T = Test group
- = Not determined

The study was performed at ToxiGenics, Inc., 1800 East Pershing Road, Decatur, IL 62526. The study was initiated on January 23, 1983 and completed on May 13, 1983.

III. Personnel

The principal technical staff involved in this study is listed below.

B. Richard Dudek, Ph.D., Study Director

Peter V. Churukian, B.A., Section Head, Chronic Inhalation Toxicology

Larry L. Horath, B.S., Section Head, Acute and Subacute Inhalation Toxicology

William J. Koretke, B.S., Inhalation Toxicology

B. Chris Pegram, B.A., Inhalation Toxicology

Patrick M. McKeown, B.S., Inhalation Toxicology

Deborah A. Reimer, B.S., Inhalation Toxicology

K. Mickle Hayward, Inhalation Toxicology

Dr. Stephen Becker, D.V.M., Pathologist

IV. Procedures

A. Test System

One-hundred forty (70 male and 70 female) rats[1] were used for the study. The animals were identified with an ear tag unique within ToxiGenics. The number and a computer readable barcode of the number were affixed to each animal's individual cage compartment. At the end of the 10-day quarantine period, 10 males and 10 females were selected for blood collection for baseline clinical chemistry and hematology determinations and then sacrificed.

Only healthy animals were used for the study as determined by body weight and clinical observations during quarantine. Six groups of 10 male and 10 female rats each were randomly selected by computer and designated as either VC-I, VC-II (Vehicle Control), T-I, T-II, T-III and T-IV. Animals were housed and exposed in 5 cubic meter chambers constructed of stainless steel and glass.

[1] Rattus norvegicus (CD rat), Charles River Breeding Laboratories, Inc., Portage, MI

During the 16-week course of the study each animal was individually housed. The cage size conformed to the standards specified in DHEW Publication (NIH) 78.23. The quarantine and study chambers were cleaned daily as specified in ToxiGenics' Standard Operating Procedures. The quarantine and study chambers were well ventilated and air-conditioned. The temperature and humidity were monitored continuously in these rooms and the light/dark cycle was 12 hours light/12 hours dark. Purina Certified Rodent Chow 5002 and filtered tap water were provided to animals ad libitum during the quarantine and study period, except during exposure. The water was assayed periodically as specified in ToxiGenics' Standard Operating Procedures. These assay records are available at ToxiGenics.

B. Test Article

A sample identified as CAB-O-SIL N70-TS, was received from the Cabot Corporation and was assigned ToxiGenics' Test Article Code Number 1/83-469. The test atmospheres were generated from the test article as received.

Additional information concerning the test article required in the FDA/GLP Regulations is not presented in this report. Excluding the safety data supplied by the Sponsor, this information was not necessary for the conduct of the study. During the study, the test material was stored in an 8.0 cubic meter inhalation chamber. The test material was considered to be stable under the conditions of storage and exposure that existed during the study.

C. Experimental Design

1. Generation of Test Atmosphere

Test atmosphere was generated by passing conditioned, compressed air through test article contained in a 1000 ml Erlenmeyer flask mounted on a dust shaker mechanism. A magnetic stir bar was used in conjunction with the shaker. The resulting air-dust mixture entered the exposure chamber at the top center and exhausted at the bottom. Also, a supply of additional air entered at the top center of each exposure chamber. The total test article used and the total airflow through the chamber was used in calculating the nominal concentration within each chamber.

Airflow was monitored by reading the pressure differential from a minihelic pressure gauge[2] and recording the corresponding airflow from a prepared calibration graph showing airflow versus differential pressure. The graph was prepared by plotting various airflow readings from an Autotronic Controls Air Flow Transducer/Digital Flow Computer[3] at various differential pressure readings and fitting a line to the points. The negative pressure of the test chamber was maintained at 0.1 inches of water. The control chamber was maintained at a positive pressure of 0.02 inches of water. Negative and positive pressures were measured with minihelic pressure gauges[2].

Particle size determinations were conducted daily for the test chamber using a Delron Cascade Impactor, Model No. DCI-6[4].

2 Dwyer Instruments, Inc., Michigan City, IN
3 Autotronic Controls Corporation, El Paso, TX
4 Delron Research Products Co., Powell, OH

The sample was collected from the breathing zone of the animals. Particle size distribution (by mass), mass median diameter, geometric standard deviation for the mass median diameter, and the calculated count median diameter were determined for each sample collected.

2. Chamber Monitoring

Gravimetric filter samples were collected from the test chamber. The gravimetric concentration was calculated by dividing the total weight of test article collected on a TF-200 Teflon Membrane Filter[5] (pore size 0.2 micrometer) by the total air sampled.

3. Exposure Conditions

The temperature of the test and control chambers were measured with an ASTM thermometer[6], and the relative humidity of the control chamber (same air supply as test chambers) was measured with a Certified Hygrometer Indicator[7]. All values were recorded regularly. The room temperature, relative humidity, and barometric pressure were recorded once during each exposure day.

4. Clinical Indices

a. In-Life Evaluations

Each animal was observed at least twice daily with respect to incidence of mortality and clinical signs. Detailed animal examinations were conducted weekly at weighings.

5 Gelman Instrument Co., Ann Arbor, MI
6 Scientific Products, Chicago, IL
7 Cole-Parmer Instrument Co., Chicago, IL

Body weights were determined for each animal weekly starting with the first exposure. A final sacrifice body weight (fasted) was obtained for each animal just prior to scheduled necropsy.

b. Clinical Pathology

All surviving animals were bled for hematology and serum chemistry determinations just prior to necropsy.

After animals were anesthetized with ether, blood samples were collected via orbital sinus puncture for hematology and serum chemistry. The following hematologic parameters were measured on whole blood samples (from baseline and subsequent sacrifice animals) treated with EDTA anti-coagulant: erythrocyte count, red cell indices, hemoglobin, packed cell volume (hematocrit), total and differential leukocyte counts. In addition, the following serum chemistry parameters were measured: glutamic pyruvic transaminase, total protein, glutamic oxaloacetic transaminase, total bilirubin, glucose, blood urea nitrogen, alkaline phosphatase.

c. Pathology

Animals found dead and sacrificed as moribund during the study, as well as scheduled sacrifice animals, were subjected to gross necropsy. The following tissues and organs were examined and all abnormal findings recorded: all external surfaces, orifices and organs; cranial cavity; carcass; external and cut surfaces of the brain; spinal cord; thoracic, pelvic and

abdominal cavities and their viscera; cervical tissues and organs.

The following organs from all animals were carefully dissected and trimmed to remove fat and other contiguous tissue and weighed: brain, kidneys, liver, heart, testes/ovaries, and lungs. In addition, the following tissues from animals designated for histological examination were processed and examined microscopically: nasal turbinates and sinuses, lungs (with mainstem bronchi) inflated with formalin, spleen, liver, kidneys, trachea, and any gross lesion(s). The tissues, organs, and identification tag from these animals were placed in individually labelled containers containing 10% buffered formalin and slowly agitated. After 12, but prior to 48 hours, the tissues were placed in fresh fixative. Nasal turbinates were prepared for histological examination over a two-week period. Tissues were trimmed to a thickness no greater than 0.4 cm for processing. Parenchymal organs were trimmed to allow the maximum possible surface area for microscopic examination. Hollow organs were trimmed and blocked to allow sectioning through the mucosa and serosa. The fixed tissues were embedded and approximately 5 micrometer sections were cut, mounted, and stained with hematoxylin/eosin. All wet tissues, tissue blocks, and slides were identified with the study number and the individual animal number.

5. Statistical Analyses

Parametric data such as body weight was analyzed using an analysis of variance (ANOVA). Statistically significant differences that were noted were further studied by either Tukey's (all groups with equal populations) or Scheffe's (unequal populations) Test of Multiple Comparison. Non-Parametric data such as organ weight ratios were analyzed using a Kruskal-Wallis ANOVA and a Test of Multiple Comparison.

V. Results

A. Exposure Conditions

Weekly time-weighted average and corresponding cumulated gravimetric concentration data for the 4-week exposure period are given below. Daily concentration data are presented in Appendix A. All daily temperature, relative humidity and barometric pressure readings are also given in Appendix A.

Week	Mean ± S.D. (mg/l air)	Cumulated Mean ± S.D. (mg/l air)
1	0.037 ± 0.016	0.037 ± 0.016
2	0.025 ± 0.004	0.031 ± 0.013
3	0.030 ± 0.002	0.031 ± 0.010
4	0.030 ± 0.004	0.031 ± 0.009

S.D. = Standard Deviation

During the first day of exposure, the time-weighted average concentration was 0.06 mg/liter of air. This resulted in the death of 9 male rats. After consulting with the Sponsor, the target concentration was set at 0.03 mg/l air for the remainder of the study. Particle size data for each of the 4 weeks of exposure as well as cumulative values are given below. Daily particle size data can be found in Appendix A.

Week	Mean	Mass Median Diameter (microns) Geometric S.D.	Cumulated Mean	Cumulated Geometric S.D.
1	0.3668	2.4749	0.3668	2.4749
2	0.2255	2.7336	0.3026	2.5925
3	0.2681	2.6178	0.2918	2.6004
4	0.2277	3.0336	0.2766	2.7035

S.D. = Standard Deviation

B. Mortality and Detailed Observations

During the 28-day exposure period 9 animals from the various designated groups were found dead on the days and times listed below.

Study Day	Time Found Dead	VC-I	VC-II	T-I	T-II	T-III	T-IV
1	AM	-	-	-	-	-	-
	PM	-	-	1	1	-	-
2	AM	-	-	2	3	1	1
	PM	-	-	-	-	-	-

NOTE: All animals found dead were males.
AM = Prior to exposure initiation.
PM = After exposure termination.
- = No deaths occurred.

These deaths apparently resulted from a time-weighted average concentration of test material equal to 0.06 mg/l of air during day 1. Subsequently, the target exposure level was lowered to 0.03 mg/l of air for the remainder of the study.

A summary of all observations noted during the 28-day study is presented in Table 1. All individual animal observations are presented in Appendix B.

TABLE 1: SUMMARY OF ANIMAL OBSERVATIONS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

Observation	Number of Occurrences (No. Males/No. Females)					
	VC-I	VC-II	T-I	T-II	T-III	T-IV
Crusty eye	0/0	0/0	0/1	0/0	1/1	1/2
Crusty muzzle	0/0	0/0	0/2	2/6	5/9	6/7
Crusty nose	0/0	2/0	4/8	6/10	9/9	9/9
Crusty substance around ear tag	1/0	1/2	0/0	0/3	0/3	2/2
Eye closed	0/0	0/0	0/0	0/0	0/0	2/1
Irregular breathing	0/0	0/0	7/9	6/10	9/10	9/10
Irritable	1/0	0/0	0/0	0/0	0/0	0/0
Lacrimation	0/0	0/0	0/0	0/1	0/0	0/0
Red stained fur	0/0	0/0	1/1	0/3	3/9	1/8
Salivation	0/0	0/0	4/0	5/2	2/1	6/0
Scab	0/0	1/0	0/0	0/0	0/2	0/0
Yellow/brown stained fur	0/0	0/0	0/0	0/0	3/1	1/1

C. Body Weights

Body weight data are summarized in Table 2. Individual body weight data are presented in Appendix C.

Mean body weights of test animals did not differ statistically from corresponding controls during the course of the study. After week 1 there was a statistically non-significant decrease in body weight gain for test animals (males and females) compared to controls. Beyond the first week and through week 4, body weight gain for test animals paralleled control weight gain. Beyond week 4 through week 16, weight gain was judged to be comparable to untreated rats of the same strain, i.e., no designated controls were available but comparisons were based on historical weight gain data for untreated control animals.

TABLE 2: SUMMARY OF MEAN BODY WEIGHT DATA

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

Sex	Interval (Week Number)	Mean Body Weights (grams) VC-I	VC-II	T-I	T-II	T-IIIA	T-IIIB	T-IV
Males	Initial	228	228	231	230	227	237	232
	1	247	249	242	230	234	237	235
	2	287	289	-	279	280	278	283
	3	-	326	-	-	311	312	321
	4	-	357	-	-	354	339	354
	5	-	-	-	-	394	371	-
	6	-	-	-	-	419	394	-
	7	-	-	-	-	445	420	-
	8	-	-	-	-	463	440	-
	9	-	-	-	-	476	450	-
	10	-	-	-	-	483	455	-
	11	-	-	-	-	-	476	-
	12	-	-	-	-	-	489	-
	13	-	-	-	-	-	492	-
	14	-	-	-	-	-	501	-
	15	-	-	-	-	-	506	-
	16	-	-	-	-	-	520	-
Final (Fasted)		267	340	228	262	460	494	336
Total Weight Change		59	129	11	49	256	283	122
Females	Initial	204	205	205	204	208	200	204
	1	206	206	201	203	202	198	200
	2	222	224	-	224	222	213	222
	3	-	238	-	-	234	225	233
	4	-	252	-	-	246	240	243
	5	-	-	-	-	266	257	-
	6	-	-	-	-	266	262	-
	7	-	-	-	-	279	274	-
	8	-	-	-	-	279	278	-
	9	-	-	-	-	281	282	-
	10	-	-	-	-	281	284	-
	11	-	-	-	-	-	290	-
	12	-	-	-	-	-	292	-
	13	-	-	-	-	-	297	-
	14	-	-	-	-	-	304	-
	15	-	-	-	-	-	304	-
	16	-	-	-	-	-	308	-
Final (Fasted)		208	241	191	217	268	296	235
Total Weight Change		18	47	-4	20	73	108	39

D. Clinical Pathology

1. Hematology

Summaries of final hematology data are presented in Tables 4 and 5 for males and females, respectively. Individual animal data (including baselines) are presented in Appendix D. Baseline summary data are presented in Table 3.

Significant changes in blood cellular constituents attributable to exposure to CAB-O-SIL N70-TS were detected in both sexes. At study week four, there was an increase in the total leukocyte count and at study week two and four there was a statistically significant increase in the relative number of neutrophils and a statistically significant decrease in the relative number of lymphocytes. These findings are consistent with the chronic-active pulmonary inflammatory process seen histologically.

2. Serum Chemistry

Summaries of final serum chemistry data are presented in Tables 4 and 5 for males and females, respectively. Individual animal data (including baselines) are presented in Appendix E. Baseline summary data are presented in Table 3.

At study week four, there was approximately a 20% increase in serum glutamic oxaloacetic transaminase (SGOT), an enzyme when elevated in the serum is generally associated with hepatic injury. Other indicators of liver function were not remarkably different from their Vehicle Control counterparts. The increased SGOT level is not assigned biological significance.

Control animals were not available for either of the recovery groups but the total leukocyte data for these two test groups were judged to be normal although the shift in cell types present, described above, continued to be observed, and perhaps even exacerbated.

TABLE 3: SUMMARY OF CLINICAL PATHOLOGY DATA - BASELINE

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	Males	Females
Hematology		
Erythrocytes (mil/mm^3)	6.8	7.5
Hemoglobin (g/dl)	15.7	16.6
Hematocrit (%)	40.8	41.9
Mean Corpuscular Volume (u^3)	60	56
Mean Corpuscular Hemoglobin (Pg)	23	22
Mean Corpuscular Hemoglobin Concentration (%)	38	39
Leukocytes (thous/mm^3)	13.5	10.7
Banded Neutrophils (#/100 cells)	0	0
Segmented Neutrophils (#/100 cells)	12	12
Lymphocytes (#/100 cells)	87	87
Eosinophils (#/100 cells)	1	0
Basophils (#/100 cells)	0	0
Monocytes (#/100 cells)	0	0
Serum Chemistry		
Glucose (mg/dl)	122	125
Blood Urea Nitrogen (mg/dl)	15	17
Glutamic Oxaloacetic Transaminase (IU/l)	79	62
Glutamic Pyruvic Transaminase (IU/l)	27	24
Alkaline Phosphatase (IU/l)	182	109
Total Bilirubin (mg/dl)	0.31	0.25
Total Protein (g/dl)	5.8	6.2

TABLE 4: SUMMARY OF CLINICAL PATHOLOGY DATA - MALES

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	VC-I	VC-II	T-I	T-II	T-IIIA	T-IIIB	T-IV
Hematology							
Erythrocytes (mil/mm^3)	7.5	7.7	7.4	7.5	8.3	8.7	7.9
Hemoglobin (g/dl)	16.0	16.5	16.2	16.1	16.4	16.8	16.9
Hematocrit (%)	42.7	43.8	44.3	42.9	40.7	43.2	44.7
Mean Corpuscular Volume (M^3)	57	57	60	57	49.4	50	57
Mean Corpuscular Hemoglobin (Pg)	21	21	22	21	20	19.4	21
Mean Corpuscular Hemoglobin Concentration (%)	37	37	36	37	40	38.6	37
Leukocytes (thous/mm^3)	9	10	11	10	9	10	12*
Banded Neutrophils (#/100 cells)	0	0	0	0	0	0	0
Segmented Neutrophils (#/100 cells)	15	17	23	23*	25	26	27**
Lymphocytes (#/100 cells)	85	83	77	77*	74	72	73**
Eosinophils (#/100 cells)	1	0	0	0*	1	1	0
Basophils (#/100 cells)	0	0	0	0	0	0	0
Monocytes (#/100 cells)	0	0	0	0	0	1	0
Serum Chemistry							
Glucose (mg/dl)	131	146	135	144	143	137	142
Blood Urea Nitrogen (mg/dl)	16	17	13	16	13	18	19
Glutamic Oxaloacetic Transaminase (IU/l)	72	74	70	76	71	63	73
Glutamic Pyruvic Transaminase (IU/l)	26	28	25	27	23	25	29
Alkaline Phosphatase (IU/l)	161	131	158	175	77	61	138
Total Bilirubin (mg/dl)	0.30	0.30	0.25	0.32	0.30	0.23	0.29
Total Protein (g/dl)	5.7	5.9	5.9	5.7	6.6	6.9	6.2

* Statistically significant difference from the VC group at the 95% level of confidence ($p<0.05$).
** Statistically significant difference from the VC group at the 99% level of confidence ($p<0.01$).
NOTE: Only two sets of test groups can be compared statistically; VC-I with T-II (both sacrificed after 2 weeks) and VC-II with T-IV (both sacrificed after 4 weeks).

TABLE 5: SUMMARY OF CLINICAL PATHOLOGY DATA - FEMALES

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	VC-I	VC-II	T-I	T-II	T-IIIA	T-IIIB	T-IV
Hematology							
Erythrocytes (mil/mm^3)	7.7	7.6	7.5	7.5	7.8	8.0	7.9
Hemoglobin (g/dl)	16.4	16.4	16.3	16.0	16.6	16.7	16.9
Hematocrit (%)	43.0	42.7	43.8	42.0	41.3	43.0	43.8
Mean Corpuscular Volume (M^3)	56	56	59	56	53	54	55
Mean Corpuscular Hemoglobin (Pg)	21	21	22	21	21	21	21
Mean Corpuscular Hemoglobin Concentration (%)	38	38	37	38	40	39	38
Leukocytes (thous/mm^3)	9	9	9	9	8	7	12**
Banded Neutrophils (#/100 cells)	0	0	0	0	0	0	0
Segmented Neutrophils (#/100 cells)	17	17	21	32**	27	30	29**
Lymphocytes (#/100 cells)	81	83	78	68**	73	67	70**
Eosinophils (#/100 cells)	2	1	1	1*	1	3	1
Basophils (#/100 cells)	0	0	0	0	0	0	0
Monocytes (#/100 cells)	0	0	0	0	0	0	0
Serum Chemistry							
Glucose (mg/dl)	125	136	129	131	135	137	137
Blood Urea Nitrogen (mg/dl)	18	21	17	19	18	16.4	21
Glutamic Oxaloacetic Transaminase (IU/l)	71	59	66	65	52	194	71**
Glutamic Pyruvic Transaminase (IU/l)	27	27	25	28	22	121	30
Alkaline Phosphatase (IU/l)	83	74	82	91	47	27	72
Total Bilirubin (mg/dl)	0.27	0.28	0.23	0.29	0.27	0.26	0.26
Total Protein (g/dl)	6.2	6.6	6.1	6.3	7.5	7.8	6.9

* Statistically significant difference from the VC group at the 95% level of confidence ($p<0.05$).
** Statistically significant difference from the VC group at the 99% level of confidence ($p<0.01$).
NOTE: Only two sets of test groups can be compared statistically; VC-I with T-II (both sacrificed after 2 weeks) and VC-II with T-IV (both sacrificed after 4 weeks).

E. Pathology

1. Gross Pathology

The individual necropsy findings are detailed in Appendix G and summarized in Table 6. The predominant macroscopic finding associated with exposure to CAB-O-SIL N70-TS was pulmonary discoloration. At study week one, 2/7 T-I male rats had a mottled discoloration of the lung present. At study week two, 8/16 T-II rats had a diffuse red to grey discoloration present. At study week four, 17/19 of the sacrificed animals showed either a mottled or diffuse pulmonary discoloration. By recovery week six, a more localized pattern of discoloration was evident in 10/10 of the sacrificed rats and at recovery week twelve a localized pattern of discoloration was seen in 6/9 of the lungs and a more diffuse pattern was evident in 3/9 of the lungs.

Other observed macroscopic changes were seen in both control and test animals but none appeared to be related to CAB-O-SIL N70-TS exposure.

TABLE 6: SUMMARY OF NECROPSY FINDINGS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS FOR 1, 2, 3, AND 4 WEEKS OF EXPOSURE

TEST ARTICLE: CAB-O-SIL N70-TS

Location	VC-I Male No.	VC-I Male (%)	VC-I Female No.	VC-I Female (%)	VC-II Male No.	VC-II Male (%)	VC-II Female No.	VC-II Female (%)	T-I Male No.	T-I Male (%)	T-I Female No.	T-I Female (%)
BRONCHIAL LYMPH NODE												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Enlarged, solitary or multiple, pale or gray red	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
EAR												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	9	(90)	10	(100)	7	(100)	10	(100)
Discoloration, solitary, red brown, right, crusted, tip of ear	0	(0)	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)
EXTERNAL SURFACE												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	9	(90)	10	(100)	8	(80)	9	(90)	5	(71)	3	(30)
Exudation, diffuse, brown or tan, around ear tag	1	(10)	0	(0)	1	(10)	1	(10)	0	(0)	0	(0)
Exudation, diffuse, brown, red, red brown, or black, nasal region or nasal and ocular regions, crusted, mild	0	(0)	0	(0)	1	(10)	0	(0)	2	(29)	7	(70)
KIDNEYS												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	9	(90)
Dilated/distended, bilateral or right, pelvis	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(10)
Stone, solitary, white or yellow, right	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
LUNG												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	8	(80)	8	(80)	6	(60)	9	(90)	2	(29)	6	(60)
Adhesion, solitary, white, right middle lobe to thoracic wall	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Discoloration, diffuse, red, red gray, or gray	2	(20)	1	(10)	1	(10)	0	(0)	0	(0)	0	(0)
Discoloration, multiple focal, pale, white or gray	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Depression, diffuse, red, gray	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	2	(20)

TABLE 6 (continued): SUMMARY OF NECROPSY FINDINGS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS FOR 1, 2, 3, AND 4 WEEKS OF EXPOSURE

TEST ARTICLE: CAB-O-SIL N70-TS

Location	VC-I Male No.	VC-I Male (%)	VC-I Female No.	VC-I Female (%)	VC-II Male No.	VC-II Male (%)	VC-II Female No.	VC-II Female (%)	T-I Male No.	T-I Male (%)	T-I Female No.	T-I Female (%)
LUNG (continued)												
Discoloration, solitary or multiple focal, red	0	(0)	1	(10)	3	(30)	1	(10)	3	(43)	2	(20)
Mottled, diffuse, pale, pale tan, pale red, pale red tan, red tan, or red gray	0	(0)	0	(0)	0	(0)	0	(0)	2	(29)	0	(0)
Not collapsed	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(10)
LYMPH NODE												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Discoloration, multiple, red, cervical region	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Enlarged, multiple, pale, abdominal cavity	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
SKIN												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	9	(90)	10	(100)	7	(100)	10	(100)
Discoloration, multiple focal, brown, bilateral femoral region, crusted	0	(0)	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)
SPLEEN												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Cyst, solitary, red, surface	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Misshaped, mild	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
URETERS												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Dilated/distended, bilateral, moderate	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Stone, solitary, white, left	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)

TABLE 6 (continued): SUMMARY OF NECROPSY FINDINGS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS FOR 1, 2, 3, AND 4 WEEKS OF EXPOSURE

TEST ARTICLE: CAB-O-SIL N70-TS

Location	VC-I Male No.	VC-I Male (%)	VC-I Female No.	VC-I Female (%)	VC-II Male No.	VC-II Male (%)	VC-II Female No.	VC-II Female (%)	T-I Male No.	T-I Male (%)	T-I Female No.	T-I Female (%)
URINARY BLADDER												
Number Examined	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Normal	10	(100)	10	(100)	10	(100)	10	(100)	7	(100)	10	(100)
Stone, multiple, white	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
UTERUS												
Number Examined	-	-	10	(100)	-	-	10	(100)	-	-	10	(100)
Normal			10	(100)			10	(100)			10	(100)
Tissue mass, solitary, red, right, firm			0	(0)			0	(0)			0	(0)

TABLE 6 (continued): SUMMARY OF NECROPSY FINDINGS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS FOR 1, 2, 3, AND 4 WEEKS OF EXPOSURE

TEST ARTICLE: CAB-O-SIL N70-TS

Location	T-II Male No. (%)	T-II Female No. (%)	T-IIIA Male No. (%)	T-IIIA Female No. (%)	T-IIIB Male No. (%)	T-IIIB Female No. (%)	T-IV Male No. (%)	T-IV Female No. (%)
BRONCHIAL LYMPH NODE								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	5 (83)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	6 (67)	6 (60)
Enlarged, solitary or multiple, pale or gray red	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (33)	4 (40)
EAR								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Discoloration, solitary, red brown, right, crusted, tip of ear	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
EXTERNAL SURFACE								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	3 (50)	1 (10)	5 (100)	5 (100)	4 (100)	5 (100)	4 (44)	4 (40)
Exudation, diffuse, brown or tan, around ear tag	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	2 (20)
Exudation, diffuse, brown, red, red brown, or black, nasal region or nasal and ocular regions, crusted, mild	3 (50)	9 (90)	0 (0)	0 (0)	0 (0)	0 (0)	4 (44)	5 (50)
KIDNEYS								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	4 (80)	5 (100)	3 (75)	5 (100)	8 (89)	9 (90)
Dilated/distended, bilateral or right, pelvis	0 (0)	0 (0)	1 (20)	0 (0)	1 (25)	0 (0)	1 (11)	1 (10)
Stone, solitary, white or yellow, right	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	1 (11)	0 (0)
LUNG								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	2 (33)	2 (20)	0 (0)	0 (0)	1 (25)	0 (0)	1 (11)	1 (10)
Adhesion, solitary, white, right middle lobe to thoracic wall	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)

TABLE 6 (continued): SUMMARY OF NECROPSY FINDINGS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS FOR 1, 2, 3, AND 4 WEEKS OF EXPOSURE

TEST ARTICLE: CAB-O-SIL M70-TS

Location	T-II Male No. (%)	T-II Female No. (%)	T-IIIA Male No. (%)	T-IIIA Female No. (%)	T-IIIB Male No. (%)	T-IIIB Female No. (%)	T-IV Male No. (%)	T-IV Female No. (%)
LUNG (continued)								
Discoloration, diffuse, red, red gray, or gray	2 (33)	6 (60)	1 (20)	1 (20)	1 (25)	2 (40)	0 (0)	2 (20)
Discoloration, multiple focal, pale, white or gray	0 (0)	0 (0)	5 (100)	5 (100)	2 (50)	4 (80)	1 (11)	0 (0)
Discoloration, solitary or multiple focal, red	2 (33)	2 (20)	4 (80)	0 (0)	1 (25)	0 (0)	1 (11)	0 (0)
Mottled, diffuse, pale, pale tan, pale red, pale red tan, red tan, or red gray	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (78)	7 (70)
Not collapsed	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
LYMPH NODE								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	5 (100)	5 (100)	3 (75)	5 (100)	8 (89)	10 (100)
Discoloration, multiple, red, cervical region	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)
Enlarged, multiple, pale, abdominal cavity	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)
SKIN								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Discoloration, multiple focal, brown, bilateral femoral region, crusted	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SPLEEN								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	4 (80)	5 (100)	4 (100)	5 (100)	9 (100)	9 (90)
Cyst, solitary, red, surface	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)
Misshaped, mild	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (00

TABLE 6 (continued): SUMMARY OF NECROPSY FINDINGS

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS FOR 1, 2, 3, AND 4 WEEKS OF EXPOSURE

TEST ARTICLE: CAB-O-SIL N70-TS

Location	T-II Male No. (%)	T-II Female No. (%)	T-IIIA Male No. (%)	T-IIIA Female No. (%)	T-IIIB Male No. (%)	T-IIIB Female No. (%)	T-IV Male No. (%)	T-IV Female No. (%)
URETERS								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	5 (100)	5 (100)	3 (75)	5 (100)	8 (89)	10 (100)
Dilated/distended, bilateral, moderate	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	1 (11)	0 (0)
Stone, solitary, white, left	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)
URINARY BLADDER								
Number Examined	6 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)	9 (100)	10 (100)
Normal	6 (100)	10 (100)	5 (100)	5 (100)	3 (75)	5 (100)	8 (89)	10 (100)
Stone, multiple, white	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	1 (11)	0 (0)
UTERUS								
Number Examined	- -	10 (100)	- -	5 (100)	- -	5 (100)	- -	10 (100)
Normal		9 (90)		5 (100)		5 (100)		10 (100)
Tissue mass, solitary, red, right, firm		1 (10)		0 (0)		0 (0)		0 (0)

2. Organ Weights

Organ weight data are summarized in Tables 7 and 8. Individual organ weight data are presented in Appendix F.

T-II and T-IV males showed statistically increased lung weights compared to VC-I and VC-II, respectively. The increased lung weights are of biological significance and appear to be related to the microscopic lesions seen histologically.

T-II and T-IV females showed a similar statistically and biologically significant increase in lung weights compared to VC-I and VC-II, respectively. Statistically increased T-IV female brain weights are not assigned biological significance. Similarly the decreased spleen weights of T-IV females compared to VC-II is not assigned biological significance.

Overall, organ weight data indicate the lung as the target organ in both sexes. The decrease in lung weights seen in T-IIIA males and T-III A females (exposed for 4 weeks followed by 6 weeks of recovery) and T-IIIB females (exposed for 4 weeks followed by 12 of recovery) compared to T-IV, may be indicative of the less fulminate condition seen in recovery animals histologically.

TABLE 7: SUMMARY OF ORGAN WEIGHT DATA - MALES

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	VC-I	VC-II	T-I	T-II	T-IIIA	T-IIIB	T-IV
Organ Weight (grams)							
Brain	1.97	2.02	1.91	1.95	2.08	2.21	2.05
Heart	1.26	1.45	1.15	1.23	1.74	1.60	1.33
Liver	9.07	11.1	7.98	8.94	13.5	13.8	10.7
Kidneys	2.47	2.93	2.16	2.54	3.18	3.61	2.86
Lung	1.69	1.78	2.00	2.12**	2.51	3.49	2.93**
Testicles	2.97	3.04	2.57	3.08	3.46	3.12	2.80
Spleen	0.66	0.70	0.51	0.65	0.78	0.70	0.72
Organ/Body Weight Ratio (g/100g)							
Brain	0.74	0.59	0.84	0.75	0.46	0.45	0.61
Heart	0.47	0.43	0.50	0.47	0.38	0.32	0.40
Liver	3.39	3.27	3.50	3.41	2.93	2.83	3.17
Kidneys	0.93	0.86	0.95	0.97	0.69	0.74	0.86
Lung	0.63	0.52	0.89	0.81**	0.55	0.69	0.87**
Testicles	1.11	0.90	1.13	1.18	0.76	0.64	0.84
Spleen	0.25	0.21	0.22	0.25	0.17	0.14	0.22
Organ/Brain Weight Ratio (g/g)							
Heart	0.64	0.72	0.60	0.63	0.83	0.73	0.65
Liver	4.60	5.53	4.18	4.58	6.47	6.26	5.20
Kidneys	1.26	1.45	1.14	1.30	1.52	1.64	1.40
Lung	0.86	0.88	1.05	1.08**	1.20	1.58	1.43**
Testicles	1.51	1.52	1.35	1.58	1.66	1.41	1.36*
Spleen	0.33	0.35	0.27	0.33	0.37	0.32	0.35

* Statistically significant difference from the VC group at the 95% level of confidence ($p<0.05$).
** Statistically significant difference from the VC group at the 99% level of confidence ($p<0.01$).
NOTE: Only two sets of test groups can be compared statistically; VC-I with T-II (both sacrificed after 2 weeks) and VC-II with T-IV (both sacrificed after 4 weeks).

TABLE 8: SUMMARY OF ORGAN WEIGHT DATA - FEMALES

28-DAY DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	VC-I	VC-II	T-I	T-II	T-IIIA	T-IIIB	T-IV
Organ Weight (grams)							
Brain	1.89	1.86	1.83	1.87	1.91	2.02	1.96*
Heart	1.04	1.07	0.91	1.06	1.02	1.15	1.06
Liver	7.01	7.36	6.26	7.53	7.23	8.01	7.12
Kidneys	1.95	1.99	1.67	1.88	1.70	2.02	1.90
Lung	1.50	1.48	2.14	2.17**	2.11	2.03	2.69**
Ovaries	0.09	0.10	0.08	0.09	0.08	0.05	0.11
Spleen	0.55	0.65	0.50	0.62	0.52	0.51	0.54**
Organ/Body Weight Ratio (g/100g)							
Brain	0.91	0.78	0.96	0.86	0.72	0.69	0.83*
Heart	0.50	0.44	0.48	0.49	0.38	0.39	0.45
Liver	3.36	3.05	3.28	3.46	2.71	2.71	3.03
Kidneys	0.94	0.83	0.87	0.86*	0.64	0.69	0.81
Lung	0.72	0.62	1.13	1.00**	0.79	0.69	1.14**
Ovaries	0.05	0.04	0.04	0.04	0.03	0.02	0.05
Spleen	0.26	0.27	0.26	0.28	0.19	0.17	0.23**
Organ/Brain Weight Ratio (g/g)							
Heart	0.55	0.57	0.50	0.57	0.53	0.57	0.54
Liver	3.70	3.95	3.43	4.05	3.78	3.97	3.64*
Kidneys	1.03	1.07	0.91	1.01	0.89	1.00	0.97*
Lung	0.79	0.80	1.17	1.16**	1.10	1.01	1.38**
Ovaries	0.05	0.05	0.04	0.05	0.04	0.02	0.06
Spleen	0.29	0.35	0.27	0.33	0.27	0.25	0.28**

* Statistically significant difference from the VC group at the 95% level of confidence ($p<0.05$).
** Statistically significant difference from the VC group at the 99% level of confidence ($p<0.01$).
NOTE: Only two sets of test groups can be compared statistically; VC-I with T-II (both sacrificed after 2 weeks) and VC-II with T-IV (both sacrificed after 4 weeks).

3. Histopathology

The microscopic findings for the tissues examined by animal are detailed in Appendix G and summarized in Tables 9 and 10. The lungs were examined from five rats that died during the first 2 days of the study, from five T-II rats and from five VC-I rats. (Findings summarized in Table 9.) Lung, liver, kidney, three sections of nasal turbinates and sinuses, spleen, trachea and any macroscopically abnormal tissues were examined from all surviving VC-II, T-IV, T-IIIA, and T-IIIB rats. (Findings summarized in Table 10.) In addition, these tissues were examined in the one T-IV male rat (AE1417) found dead. (Findings not summarized but available in Appendix G.)

In all test groups the target organ was the lung. Although a variety of diagnoses were made on the other tissues examined, all appeared to be unrelated to exposure to CAB-O-SIL N70-TS. Examination of lung tissue with polarized light proved unbeneficial.

A lethal, acute pulmonary hemorrhage accompanied by bronchiolar plugs with emphysema was seen in all (5/5) of the examined animals dying on test day 1 or 2 (0.06 mg/l). Comparatively, the lungs from the T-II grcup (sacrificed at week 2) showed a chronic-active interstitial/alveolar inflammation, multifocal in distribution, often surrounding areas of emphysema (5/5). Marked pulmonary consolidation was seen in one of these rats.

All of the T-IV (sacrificed at week 4) rats, regardless of sex, had a mild to very severe pulmonary chronic

interstitial/alveolar consolidative lesion usually diffuse in distribution. Elements of this lesion suggested an active process; namely the occurrence of alveolar foam cells (pulmonary macrophages), a protein rich alveolar transudate, and an interstitial edema with prominent interstitial macrophages.

In the 6-week recovery group (T-IIIA), the previously described chronic-active pulmonary disease had progressed to a less fulminant but still active lesion characterized by the presence of alveolar foam cells (pulmonary macrophages) and interstitial thickening and consolidation. Physiologically, this lesion would be expected to be of less consequence than those previously described since there was minimal emphysema and more localization of the changes.

In the 12-week recovery group (T-IIIB), localized areas of aggregated pulmonary macrophages were seen in alveoli interlaced by a thickened fibrotic interstitium (9/9). Occasionally (4/9), there was judged to be a minimal to mild collagenous proliferative component in this involved interstitium.

TABLE 9: SUMMARY OF HISTOPATHOLOGIC FINDINGS/COMPARISON OF VC-I, T-II (FINAL SACRIFICE), AND FOUND DEAD RATS

SUBCHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	Final Sacrifice						Found Dead*	
	VC-I Male		VC-I Female		T-II Male		T-II Female		Male	
Organ or Tissue	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
BRONCHIAL LYMPH NODE										
Number Examined	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)
Not Remarkable	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Hyperemia, medullary sinus, mild	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)
LUNG										
Number Examined	2	(100)	3	(100)	1	(100)	4	(100)	5	(100)
Not Remarkable	1	(50)	3	(100)	0	(0)	0	(0)	0	(0)
Cellular infiltrate, bronchiolar, mild	0	(0)	0	(0)	1	(100)	2	(50)	0	(0)
Cellular infiltrate, bronchiolar, moderate	0	(0)	0	(0)	0	(0)	2	(50)	0	(0)
Foam cells, interstitial, alveolar, moderate	0	(0)	0	(0)	0	(0)	4	(100)	0	(0)
Foam cells, interstitial, alveolar, severe	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)
Atelectasis, moderate	0	(0)	0	(0)	1	(100)	3	(75)	0	(0)
Atelectasis, interstitial, severe	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
Emphysema, alveolar, minimal	0	(0)	0	(0)	1	(100)	1	(25)	0	(0)
Emphysema, alveolar, moderate	0	(0)	0	(0)	0	(0)	2	(50)	0	(0)
Pneumonitis, interstitial, subpleural, minimal	1	(50)	0	(0)	0	(0)	0	(0)	0	(0)
Consolidation, interstitial, mild	0	(0)	0	(0)	1	(100)	1	(25)	0	(0)
Consolidation, interstitial, moderate	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
Consolidation, alveolar, severe	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
Hemorrhage, alveolar, bronchiolar, moderate	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
Hemorrhage, alveolar, bronchiolar, severe	0	(0)	0	(0)	0	(0)	0	(0)	4	(80)
Foam cells, alveolar, mild	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
Foam cells, alveolar, moderate	0	(0)	0	(0)	0	(0)	0	(0)	2	(40)

* Only males were found dead.
NOTE: A random sampling of 5 animals from each of the VC-I, T-II, and Found Dead groups was examined histologically.

TABLE 9 (continued): SUMMARY OF HISTOPATHOLOGIC FINDINGS/COMPARISON OF VC-I, T-II (FINAL SACRIFICE), AND FOUND DEAD RATS

SUBCHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS

TEST ARTICLE: CAB-O-SIL N70-TS

	Final Sacrifice								Found Dead*	
	VC-I Male		VC-I Female		T-II Male		T-II Female		Male	
Organ or Tissue	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Hyperemia, interstitial, moderate	0	(0)	0	(0)	0	(0)	0	(0)	3	(60)
Hyperemia, interstitial, severe	0	(0)	0	(0)	0	(0)	0	(0)	2	(40)
Bronchiolitis, mild	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
Bronchiolitis, moderate	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
Bronchiolitis, severe	0	(0)	0	(0)	0	(0)	0	(0)	3	(60)
Emphysema, alveolar, moderate	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
Emphysema, alveolar, severe	0	(0)	0	(0)	0	(0)	0	(0)	4	(80)
Pneumonitis, interstitial, subpleural, minimal	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
Pneumonitis, subpleural, minimal	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)

* Only males were found dead.
NOTE: A random sampling of 5 animals from each of the VC-I, T-II, and Found Dead groups was examined histologically.

TABLE 10 SUMMARY OF HISTOPATHOLOGIC FINDINGS VC-II,T-IV,T-IIIA, AND T-IIIB

SUB-CHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS
TEST ARTICLE: CAB-O-SIL M7DTS

ORGAN OR TISSUE	VC-II MALE NO.	(%)	VC-II FEMALE NO.	(%)	T-IV MALE NO.	(%)	T-IV FEMALE NO.	(%)	T-III-A MALE NO.	(%)	T-III-A FEMALE NO.	(%)	T-III-B MALE NO.	(%)	T-III-B FEMALE NO.	(%)
EAR																
NUMBER EXAMINED	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
DERMATITIS, PINNA, SEVERE	1	(100)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
KIDNEY																
NUMBER EXAMINED	10	(100)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)
NOT REMARKABLE	8	(80)	10	(100)	8	(89)	9	(90)	4	(80)	5	(100)	3	(75)	5	(100)
CYST, CORTICAL, MILD	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
GLOMERULONEPHRITIS, VERY SEVERE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
HYDRONEPHROSIS, MINIMAL	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYDRONEPHROSIS, MILD	0	(0)	0	(0)	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)
HYDRONEPHROSIS, MODERATE	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)	0	(0)	0	(0)	0	(0)
HYDRONEPHROSIS, SEVERE	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYDRONEPHROSIS, VERY SEVERE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
NEPHRITIS, INTERSTITIAL, MODERATE	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
PYELITIS, CORTICAL, PELVIC, PERIPELVIC, SEVERE	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
LIVER																
NUMBER EXAMINED	10	(100)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)
NOT REMARKABLE	7	(70)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)

TABLE 10 (Continued) SUMMARY OF HISTOPATHOLOGIC FINDINGS VC-II,T-IV,T-IIIA, AND T-IIIB

SUB-CHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS
TEST ARTICLE: CAB-O-SIL M7OTS

ORGAN OR TISSUE	VC-II MALE NO.	(%)	VC-II FEMALE NO.	(%)	T-IV MALE NO.	(%)	T-IV FEMALE NO.	(%)	T-III-A MALE NO.	(%)	T-III-A FEMALE NO.	(%)	T-III-B MALE NO.	(%)	T-III-B FEMALE NO.	(%)
LIVER(CONT)																
DEGENERATION, HEPATOCELLULAR, MILD	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
DEGENERATION, HEPATOCELLULAR, MODERATE	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
DEGENERATION, PERIPORTAL, MILD	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
LUNG																
NUMBER EXAMINED	10	(100)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)
NOT REMARKABLE	9	(90)	9	(90)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
FIBROSIS, INTERSTITIAL, MINIMAL	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	1	(20)
FIBROSIS, INTERSTITIAL, MILD	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	2	(40)
FIBROSIS, INTERSTITIAL, MODERATE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	2	(40)
FIBROSIS, INTERSTITIAL, SEVERE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
INFLAMMATION, SUBPLEURAL, MINIMAL	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
EDEMA, INTERSTITIAL, SEVERE	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
FOAM CELLS, ALVEOLAR, MODERATE	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)

42

TABLE 10 (Continued) SUMMARY OF HISTOPATHOLOGIC FINDINGS VC-II,T-IV,T-IIIA, AND T-IIIB

SUB-CHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS
TEST ARTICLE: CAB-O-SIL M7OTS

ORGAN OR TISSUE	VC-II MALE NO.	(%)	VC-II FEMALE NO.	(%)	T-IV MALE NO.	(%)	T-IV FEMALE NO.	(%)	T-III-A MALE NO.	(%)	T-III-A FEMALE NO.	(%)	T-III-B MALE NO.	(%)	T-III-B FEMALE NO.	(%)
LUNG(CONT)																
LYMPHOID HYPERPLASIA, PERIBRONCHIAL, MODERATE	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
LYMPHOID HYPERPLASIA, PERIBRONCHIAL, SEVERE	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
CONSOLIDATION, SEVERE	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
CONSOLIDATION, INTERSTITIAL, MODERATE	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
CONSOLIDATION, INTERSTITIAL, ALVEOLAR, MILD	0	(0)	0	(0)	2	(22)	0	(0)	3	(60)	1	(20)	0	(0)	0	(0)
CONSOLIDATION, INTERSTITIAL, ALVEOLAR, MODERATE	0	(0)	0	(0)	3	(33)	2	(20)	2	(40)	2	(40)	0	(0)	0	(0)
CONSOLIDATION, INTERSTITIAL, ALVEOLAR, SEVERE	0	(0)	0	(0)	4	(44)	6	(60)	0	(0)	1	(20)	0	(0)	0	(0)
CONSOLIDATION, INTERSTITIAL, ALVEOLAR, VERY SEVERE	0	(0)	0	(0)	0	(0)	2	(20)	0	(0)	0	(0)	0	(0)	0	(0)
CONSOLIDATION, ALVEOLAR, MILD	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)	0	(0)	0	(0)
ALVEOLAR PULMONARY MACROPHAGES/FOAM CELLS, MINIMAL	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	1	(20)

43

TABLE 10 (Continued) SUMMARY OF HISTOPATHOLOGIC FINDINGS VC-II,T-IV,T-IIIA, AND T-IIIB

SUB-CHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS
TEST ARTICLE: CAB-O-SIL M7DTS

ORGAN OR TISSUE	VC-II MALE NO. (%)	VC-II FEMALE NO. (%)	T-IV MALE NO. (%)	T-IV FEMALE NO. (%)	T-III-A MALE NO. (%)	T-III-A FEMALE NO. (%)	T-III-B MALE NO. (%)	T-III-B FEMALE NO. (%)
LUNG(CONT)								
ALVEOLAR PULMONARY MACROPHAGES/FOAM CELLS, MILD	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	2 (40)
ALVEOLAR PULMONARY MACROPHAGES/FOAM CELLS, MODERATE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	2 (40)
ALVEOLAR PULMONARY MACROPHAGES/FOAM CELLS, SEVERE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)
COLLAGEN PROLIFERATION, INTERSTITIAL, MINIMAL	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (50)	1 (20)
COLLAGEN PROLIFERATION, INTERSTITIAL, MILD	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)
NASAL, ORAL & PHARYNGEAL STRUCTURES								
NUMBER EXAMINED	10 (100)	10 (100)	9 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)
NOT REMARKABLE	10 (100)	9 (90)	9 (100)	10 (100)	5 (100)	5 (100)	4 (100)	5 (100)
HYPERKERATOSIS, HARD PALATE, MILD	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
OVARIES								
NUMBER EXAMINED	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)
NOT REMARKABLE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CYST, FOLLICULAR, MODERATE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
SKIN								
NUMBER EXAMINED	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
NOT REMARKABLE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

TABLE 10 (Continued) SUMMARY OF HISTOPATHOLOGIC FINDINGS VC-II,T-IV,T-IIIA, AND T-IIIB

SUB-CHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS
TEST ARTICLE: CAB-O-SIL M7OTS

ORGAN OR TISSUE	VC-II MALE NO.	(%)	VC-II FEMALE NO.	(%)	T-IV MALE NO.	(%)	T-IV FEMALE NO.	(%)	T-III-A MALE NO.	(%)	T-III-A FEMALE NO.	(%)	T-III-B MALE NO.	(%)	T-III-B FEMALE NO.	(%)
SKIN(CONT)																
DERMATITIS, MODERATE	1	(100)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
LYMPH NODE																
NUMBER EXAMINED	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYPERPLASIA, LYMPHOID, MILD	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(100)	0	(0)
SPLEEN																
NUMBER EXAMINED	10	(100)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)
NOT REMARKABLE	10	(100)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	4	(80)
HEMOSIDERIN DEPOSITIONS, MINIMAL	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(20)
THYMUS																
NUMBER EXAMINED	0	(0)	0	(0)	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)	0	(0)	0	(0)
TRACHEA																
NUMBER EXAMINED	10	(100)	10	(100)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)
NOT REMARKABLE	10	(100)	9	(90)	9	(100)	10	(100)	5	(100)	5	(100)	4	(100)	5	(100)
INFLAMMATION, SUBMUCOSA, MINIMAL	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
URETER																
NUMBER EXAMINED	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYPERPLASIA, EPITHELIAL, MODERATE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(100)	0	(0)

TABLE 10 (Continued) SUMMARY OF HISTOPATHOLOGIC FINDINGS VC-II,T-IV,T-IIIA, AND T-IIIB

SUB-CHRONIC DUST INHALATION TOXICITY STUDY IN ALBINO RATS
TEST ARTICLE: CAB-O-SIL M7DTS

ORGAN OR TISSUE	VC-II MALE NO.	(%)	VC-II FEMALE NO.	(%)	T-IV MALE NO.	(%)	T-IV FEMALE NO.	(%)	T-III-A MALE NO.	(%)	T-III-A FEMALE NO.	(%)	T-III-B MALE NO.	(%)	T-III-B FEMALE NO.	(%)
URETER(CONT)																
HYPERPLASIA, EPITHELIAL, SEVERE	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
DILATATION, SEVERE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(100)	0	(0)
URINARY BLADDER																
NUMBER EXAMINED	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYPERPLASIA, EPITHELIAL, MODERATE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(100)	0	(0)
HYPERPLASIA, MUCOSAL, SEVERE	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
CAST, PROTEINACEOUS	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(100)	0	(0)
MESENTERIC LYMPH NODE																
NUMBER EXAMINED	0	(0)	0	(0)	1	(11)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYPERPLASIA, LYMPHOID, MILD	0	(0)	0	(0)	1	(100)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
BRONCHIAL LYMPH NODE																
NUMBER EXAMINED	0	(0)	0	(0)	3	(33)	5	(50)	0	(0)	0	(0)	0	(0)	0	(0)
NOT REMARKABLE	0	(0)	0	(0)	0	(0)	1	(20)	0	(0)	0	(0)	0	(0)	0	(0)
HYPERPLASIA, FOLLICULAR, LYMPHOID, MODERATE	0	(0)	0	(0)	1	(33)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
HYPERPLASIA, LYMPHOID, MILD	0	(0)	0	(0)	2	(67)	4	(80)	0	(0)	0	(0)	0	(0)	0	(0)

VI. List of Appendices

Appendix	Description
A	Exposure Conditions
B	Mortality and Detailed Observations
C	Body Weight Data
D	Hematology Data
E	Serum Chemistry Data
F	Organ Weight Data
G	Pathology

Abbreviations

FD - Found Dead

FS - Final Sacrifice

MODH - Moderate Hemolysis

N - Number

RS - Recovery Sacrifice

SC - Sample Clotted

SD - Standard Deviation

SLTH - Slight Hemolysis

W - Week

END